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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/646,363	ZENG, XIAN-MING	
	Examiner	Art Unit	
	JAMES H. ALSTRUM ACEVEDO	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 5-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/17/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-3 and 5-19 are pending. Applicant has amended claims 1, 6-9, and 11-12. Applicant has cancelled claim 4. Receipt and consideration of Applicant's amended claims and remarks/arguments, submitted on December 12, 2007 are acknowledged. All rejections not explicitly maintained in the instant office action have been withdrawn per Applicants' claim amendments.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-9 and 12 **remain rejected** under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons of record restated below. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 6-9 and 12 of the instant application claim a method of preparing a dry powder inhalation composition comprising (i) a 1st particulate medicament (e.g. an antiinflammatory steroid, such as budesonide) or a pharmaceutically acceptable salt, solvate[1], or salt solvate thereof and (ii) a 2nd particulate medicament (e.g. a bronchodilator, such as formoterol) or a pharmaceutically acceptable salt, solvate, or salt solvate thereof. The instant specification does not disclose, to which solvates or

[1] Applicant indicates that solvate includes hydrates, but does not define the term solvate to be limited to hydrates.

salt solvates of the 1st and 2nd particulate medicaments Applicants are referring. In paragraph [0029], Applicant indicates that the term solvate is inclusive of hydrates, but does not define solvate to be limited to hydrates. The only specific salt solvate mentioned in Applicant's specification is "formoterol fumarate dihydrate", mentioned in paragraph [0030] of Applicant's specification. No other salt solvates are disclosed in Applicant's specification. It is generally accepted in the art that the formation of a particular solvate or hydrate for a given compound or series of compounds is unpredictable (see Vippagunta et al. "Crystalline Solids," *Advanced Drug Delivery Reviews*, **2001**, *48*, pp 18), therefore, the generic reference to a solvate of anti-inflammatory steroids, bronchodilators, formoterol, 1st particulate medicament, or 2nd particulate medicament in the instant specification **does not provide adequate written support for claims drawn to any solvate or hydrate of these compounds, with the exception of formoterol fumarate**.

Response to Arguments

Applicant's arguments filed July 7, 2008 have been fully considered but they are not persuasive. Applicants have traversed the instant rejection by arguing that (1) the specification allegedly enables formulations comprising any solvate or hydrate of any bronchodilator and any anti-inflammatory steroid; (2) the Vippagunta reference allegedly supports Applicants' belief that one can allegedly produce every solvate and hydrate of any bronchodilator or anti-inflammatory steroid; and (3) solvates and hydrates are allegedly predictable per Applicants' reading of Vippagunta.

The Examiner respectfully disagrees with Applicants' traversal arguments. Regarding (1), the instant rejection is a written description rejection, thus arguments as to alleged enablement are irrelevant. Furthermore, the only specific solvate disclosed by Applicants' specification is formoterol fumarate monohydrate. It is incredulous for Applicants to argue that their specification provides written support for all solvates and hydrates of all bronchodilators and all anti-inflammatory steroids without identifying a single solvate or hydrate, excluding formoterol fumarate monohydrate, or disclosing how one can obtain any particular solvate or hydrate.

Regarding (2)-(3), Applicants have misread and mischaracterized the teachings of Vippagunta. Vippagunta indicates that the primary focus of research has been the characterization of known polymorphs (pgs. 7-9) and that attempts are also being made to develop means of predicting polymorphs. Vippagunta explicitly states, "The main challenge in managing the phenomenon of multiple solid forms [i.e. polymorphs] of a drug is ***the inability to predict* the number of forms that can be expected**" (pg. 11, "Prediction of Polymorphs"). Vippagunta concludes the "Prediction of Polymorphs" section by stating, "Hence, no general method is currently available for the prediction or interpretation of the properties of complicated polymorphic and pseudopolymorphic systems [i.e. solvates and hydrates are pseudopolymorphs]." (*Id.* at 12). Specifically concerning solvates and hydrates, Vippagunta states, "There may be too many possibilities so that **no computer programs are currently available for predicting the crystal structures of solvates and hydrates** (pg. 18, sentence bridging left and right columns). Thus, Vippagunta clearly states that the prediction of solvates and hydrates is not possible. Applicants provide no description of how one may predict the

existence of any solvate or hydrate, do not disclose how to make any solvate or hydrate, or identify any solvates or hydrates by name or chemical structure, except for formoterol fumarate monohydrate. In conclusion, Applicants have failed to demonstrate that their specification provides sufficient written description to allow an ordinary skilled artisan to clearly envisage any particular solvate or hydrate of any bronchodilator or any anti-inflammatory steroid, with the exclusion of formoterol fumarate monohydrate; and, an ordinary skilled artisan can only conclude that Applicants were not in possession of all solvates and all hydrates of all bronchodilators and all anti-inflammatory steroids as alleged.

Claims 6-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of preparing dry powder compositions comprising bronchodilators, anti-inflammatory steroids, formoterol fumarate monohydrate and pharmaceutically acceptable salts thereof, does not reasonably provide enablement for compositions comprising solvates, salt solvates, or hydrates of any bronchodilator or anti-inflammatory steroid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

An analysis based upon the Wands factors is set forth below.

To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In *Genentech Inc. v. Novo Nordisk* 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997); *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993),. See also *Amgen*

Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir. 1991); *In re Fisher* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Further, in *In re Wands* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court stated:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman (230 USPQ 546, 547 (Bd Pat App Int 1986)). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Breadth of Claims

Applicants' claims are broad with regards to the genera of bronchodilators anti-inflammatory steroids, and the pharmaceutically acceptable salts, solvates, salt solvates, and hydrates thereof.

Nature of the invention/State of the Prior Art

Claims 6-9 and 12 of the instant application claim a method of preparing a dry powder inhalation composition comprising (i) a 1st particulate medicament (e.g. an antiinflammatory steroid, such as budesonide) or a pharmaceutically acceptable salt, solvate[2], or salt solvate thereof and (ii) a 2nd particulate medicament (e.g. a bronchodilator, such as formoterol) or a pharmaceutically acceptable salt, solvate, or salt solvate thereof. It is generally accepted in the art that the formation of a particular solvate or hydrate for a given compound or series of compounds is unpredictable (see Vippagunta et al. "Crystalline Solids," *Advanced Drug Delivery*

[2] Applicant indicates that solvate includes hydrates, but does not define the term solvate to be limited to hydrates.

Reviews, **2001**, *48*, pp 11 and 18). Furthermore, the prediction of solvates or hydrates is not currently possible (*Id.* at 18).

Level of One of Ordinary Skill & Predictability/Unpredictability in the Art

The level of a person of ordinary skill in the art is high, with ordinary artisans having advanced medical and/or scientific degrees (e.g. M.D., Ph.D., Pharm. D. or combinations thereof). There is a general lack of predictability in the pharmaceutical art. *In re Fisher*, 427, F. 2d 833, 166, USPQ 18 (CCPA 1970). The art is especially unpredictable with regards to the existence and formation of particular polymorphs and pseudopolymorphs (e.g. hydrates and solvates) of chemical compounds, as set forth above by the teachings of Vippagunta et al.

Guidance/Working Examples

Applicants provide no guidance or working examples about the preparation of any solvate or hydrate of any bronchodilator or anti-inflammatory steroid.

In conclusion, the specification, while being enabling for methods of making dry powder compositions comprising bronchodilators, anti-inflammatory steroids, and the pharmaceutically acceptable salts thereof, does not reasonably provide enablement for methods of preparing dry powder compositions comprising solvates, salt solvates, or hydrates of any bronchodilator or anti-inflammatory steroid, with the exception of formoterol fumarate monohydrate, which is known in the prior art and commercially available.

Response to Arguments

Applicant's arguments filed July 7, 2008 have been fully considered but they are not persuasive. Applicants have traversed the instant rejection by arguing that (1) the specification allegedly enables formulations comprising any solvate or hydrate of any bronchodilator and any anti-inflammatory steroid; (2) the Vippagunta reference allegedly supports Applicants' belief that one can allegedly produce every solvate and hydrate of any bronchodilator or anti-inflammatory steroid; and (3) solvates and hydrates are allegedly predictable per Applicants' reading of Vippagunta.

These traversal arguments were addressed above in the previous written description rejection. The rebuttal to Applicants' traversal arguments is herein incorporated by reference. The instant rejection is proper.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 23-24 and 27-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 23-24 and 27-29 are indefinite because said claims recite an anti-inflammatory steroid or a bronchodilator comprising budesonide (claim 23 and 27), formoterol (claim 24), or formoterol fumarate dihydrate. Description of a single chemical compound such as a bronchodilator or anti-inflammatory as comprising renders a claim indefinite, because only a part

of the required compound is described. Thus, an ordinary skilled artisan would not be apprised of what is the required anti-inflammatory steroid or bronchodilator. Furthermore, regarding claim 29, it makes no logical sense that formoterol can comprise formoterol fumarate dihydrate. The bronchodilator known as formoterol does not contain any water molecules or fumarate moiety; thus, it is impossible for formoterol to comprise formoterol fumarate dihydrate.

Claim Rejections - 35 USC § 103

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-3 and 5-19 **remain rejected** under 35 U.S.C. 103(a) as being unpatentable over Trofast (U.S. Patent No. 6,030,604) and Keller (WO 00/28979, wherein U.S. Patent No. 6,645,466 is being used as the English language equivalent) in view of Ward et al. (U.S. Patent No. 6,616,914) for the reasons of record, which have been restated below. New claims 20-32 are appended to the instant rejection for the reasons of record. In summary, **claims 1-3 and 5-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trofast (U.S. Patent No. 6,030,604) and Keller (WO 00/28979, wherein U.S. Patent No. 6,645,466 is being used as the English language equivalent) in view of Ward et al. (U.S. Patent No. 6,616,914).**

Applicant Claims

Applicant claims (1) a method of preparing a dry powder inhalation composition comprising the steps of (a) mixing a particulate carrier with a first portion of a first particulate medicament to obtain a first mixture (b) mixing said first mixture with a second particulate medicament to obtain a second mixture, and (c) mixing said second mixture with a second portion of the first medicament to form a dry powder inhalation composition, wherein the ratio by weight of the 2nd medicament/carrier ratio is less than the ratio by weight of the 1st medicament to the carrier, wherein the particulate carrier has a VMD of from about 50 to about 250 microns and (2) a dry powder inhalation composition made utilizing a method similar to (1), wherein the composition consists of (a) said particulate carrier, (b) said 1st particulate inhalant medicament, and (c) said 2nd particulate medicament.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Keller discloses a dry powder composition with improved moisture resistance in Example 8 consisting of 0.2% w/w formoterol fumarate dihydrate (2nd med.), 0.5 % w/w glycopyrrolate (1st med.), 0.5% w/w magnesium stearate (excipient), and 98.8% w/w of lactose monohydrate (carrier) (Example 8; col. 14, lines 35-41). Both formoterol fumarate dihydrate and glycopyrrolate are known medicaments. Keller states,

> "In principle, **the constituents can be mixed with one another in any desired sequence**, where, however, mixing should expediently be carried out in such a way that the particles of the constituents--apart from the adhesion to the carrier particles--are essentially retained as such, i.e. are not destroyed, for example, by granulation and the like (col. 8, lines 53-59)."

Keller discloses that the dry powder formulations can be used in all customary dry powder inhalers and are particularly advantageously for use in **multidose dry powder inhalers** (i.e. MDPI), which contain a powder reservoir (col. 9, lines 3-8). Keller discloses that it is preferred to use magnesium stearate in dry powder formulations containing a betamimetic (e.g. formoterol), and/or an anticholinergic (e.g. glycopyrrolate), and/or a corticosteroid (e.g. budesonide) (col. 6, lines 52-54). Other suitable medicaments for use in Keller's composition are disclosed in col. 6, lines 13-33). Keller discloses that the ingress of moisture in multidose dry powder inhalers (MDPI) is a problem because it results in a dramatic fall in the in vitro fine particle dose and fine particle dose of pharmaceutical dry powders contained within said MDPI (col. 3, line 60 through col. 4, line 14).

Trofast discloses dry powder formulations for inhalation (title, abstract) that may be administered using any known dry powder inhaler, such as a **multidose inhaler**, wherein the inhaler may be a **dry powder inhaler** (col. 3, lines 20-23), and said formulations are useful for the treatment of respiratory disorders (e.g. asthma) (col. 3, lines 26-28). Trofast discloses in Example 6 a dry powder composition comprising **5.2 parts formoterol fumarate dihydrate, 896.8 parts lactose monohydrate (carrier), and 98 parts budesonide**, wherein the lactose and formoterol are mixed, micronized, and treated according to the method of WO 95/05805; budesonide is added, and the mixture is remixed, remicronized, and agglomerated. Trofast discloses that when formoterol and budesonide are present in the same dry powder formulation the molar ratio of formoterol to budesonide ranges from 1: 2,500 to 12: 1, preferably 1: 133 to 1: 6 (col. 2, lines 14-49). This corresponds to a formoterol to budesonide mass ratio, based on the molecular masses of formoterol fumarate dihydrate (496.513 g/mol) and budesonide (430.534

g/mol), ranging from approximately 1.153: 2,500 to approximately 13.8: 1, preferably from approximately 1.153: 133 to approximately 1.153: 6.

Ward teaches a method for oral and pulmonary delivery of pharmaceuticals, wherein a powder formulation for use in a dry powder inhaler (DPI) comprises a pharmaceutical, which acts as its own carrier and is present as (a) microfine particles having a diameter in the range of 1-10 microns and **larger carrier particles** that have an **average volume median diameter** of 10-2,000 microns, preferably 30-300 microns, and **most preferably from 50-100 microns in diameter**, and administration of the composition results in both a rapid onset pharmaceutical effect and a slower onset pharmaceutical effect (title; abstract; col. 2, lines 20-25 and 51-56; and claims 1-23). Ward teaches that suitable medicaments for use in the invented formulations include **beta-agonists** (i.e. a known class of bronchodilators), such as **albuterol**, **anti-inflammatories**, and **drugs for treating COPD** and other diseases (col. 4, lines 21-28). Ward teaches that the invented composition is desirable to improve patient compliance for patients taking more than one pharmaceutical (col. 1, line 60 through col. 2, line 13) and that, in general, inert carrier particles such as lactose upon inhalation administration are caught in the mouth and throat, swallowed, and exert no pharmaceutical effect (col. 3, lines 5-12).

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Trofast lacks an explicit teaching about the order of steps used in preparing the dry powders. This deficiency is cured by the teachings of Keller. Trofast lacks the teaching of

carrier particles having a volume median diameter ranging from about 50 to about 250 microns. This deficiency is cured by the teachings of Ward.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been obvious to a person of ordinary skill in the art at the time of the invention to combine the teachings of Trofast, Keller, and Ward, because all references teach dry powder formulations for inhalation administration. Per the teachings of Keller, it would have been prima facie obvious to a person of ordinary skill in the art at the time of the instant invention that one could adjust the order of mixing used to obtain an inhalable dry powder formulation. An ordinary skilled artisan cognizant of Ward 's teachings would have readily recognized that carrier particles having a volume median diameter ranging from about 50 microns to about 250 microns would be swallowed upon inhalation administration. An ordinary skilled artisan in the field of pharmaceutical formulations at the time of the instant invention (e.g. a pharmaceutical formulation scientist) would be capable of formulating an inhalable composition characterized by having a pharmaceutical effect exhibiting rapid onset properties through the use of an inert carrier, such as lactose, having a VMD ranging from 10-2,000 microns, more preferably 30-300 microns, and most preferably 50-100 microns. An ordinary skilled artisan would have had a reasonable expectation of success in modifying Trofast's invented formulations to utilize lactose carrier having an VMD ranging from 30-300 microns, because lactose is a well-known carrier used in inhalation formulations, such as the formulation taught by Trofast, and it is known in the art that inert carriers, like lactose, having a VMD from 30-300 microns are not inhaled and exert no pharmaceutical effect upon administration.

Regarding the order in which the different components are combined, Keller teaches that the different ingredients can be mixed in any desired sequence. This teaching encompasses the following sequence of steps: blending a portion of 1st active particles with carrier particles to obtain a 1st mixture; combination of a 2nd active with the 1st mixture to obtain a second mixture; and finally admixture of the remaining 1st active particles to obtain a dry powder formulation. Mixing particulate components to obtain a dry powder composition is known as demonstrated by the cited prior art references.

Regarding claim 4, the amounts of active taught by Keller and Trofast would be sufficient to form a monolayer of each of these onto the carrier particles, the amount of actives taught by both Keller and Trofast meet are sufficient to create a monolayer of active onto the carrier surface as discussed on page 10 of the office action mailed on November 13, 2006. Therefore, an ordinary skilled artisan would have had reasonable expectation that mixing of the actives in the amounts taught by both references would obviously result in a coating of at least a monolayer onto the carrier particles. Regarding the "consisting of" langauge of claim 11 and claims dependent therefrom, Trofast teaches compositions consisting solely of (a) a 1st particulate medicament, (b) a 2nd particulate medicament, and (c) a particulate carrier; Keller is relied upon solely for the teaching of the order of mixing the particulate carriers; Ward is solely relied upon for the teaching of the desirable VMD of particulate carriers used in inhalable powder formulations.

Applicant has presented data in the instant specification (Tables 1-4) demonstrating the homogeneity of dry powders produced using Applicant's claimed method. This data is not convincing regarding the patentability of the claimed method, because it lacks a comparison of

Applicant's method with the methods of the prior art. Applicant's claims 1-9 are open to a broad range of first and second medicament amounts and proportions. Even if Applicant's data in Tables 1-4 were somehow indicative of structural modification, this ground of rejection would still be proper because applicant's data was demonstrated with only 100:6 and 200:6 proportions of budesonide and formoterol fumarate dihydrate, wherein the total medicament concentration was in the range of about 5 wt%. In other words, Applicant's data is not commensurate in scope with what is being claimed in the cited claims, because these claims recite broad ranges and claim 10 is not limited to a specific 1st and 2nd medicament mixed with carrier. Claims 1-6, 8, 10, and 16-19 are readable on (i) structurally different medicaments, (ii) much higher or lower total concentrations of medicaments, and (iii) much lower or higher weight ratios of first medicament to second medicament, e.g. 100,000,000:1 or 1:0.99,999. The term "bronchodilator" may refer to a broad range of structurally different compounds (e.g. betamimetics and anticholinergics), which although exhibiting bronchodilating effects have different mechanisms of action and secondary biological activities. The term anti-inflammatory steroid" is also broad and can refer to a great variety of compounds having a steroidal core, but differing in the degree, and sometimes the kind of biological activity exhibited, in addition to anti-inflammatory effects. Similarly, claims 7 and 9 are readable on compositions with (i) structurally different 2nd medicaments (claim 7) or 1st medicaments (claim 9), (ii) much higher or lower total concentrations of medicaments, and (iii) much lower or higher weight ratios of 1st medicament to 2nd medicament. Trofast's disclosed method of mixing the composition constituents would necessarily produce a dry powder that cannot be distinguished from the dry powder encompassed by applicant's broad claim language. These data do not demonstrate that

the prior art methods do not yield dry powder formulations exhibiting the same or substantially similar physical properties/characteristics. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Response to Arguments

Applicant's arguments filed July 7, 2008 have been fully considered but they are not persuasive. Applicants traversed the instant rejection by arguing that (1) the order of the steps of the instantly claimed method is critical, as allegedly demonstrated by Applicants' data; (2) the preparation of ternary dry powder compositions is allegedly "not simple" and allegedly this assertion is supported by the prior art; (3) Ward allegedly teaches away from Applicant's invention because Ward focuses on compositions in which drug particles are function as both carrier and fine particles adsorbed onto said carrier; (4) Applicant has identified a problem of forming a ternary mixture representing a long-felt need that Applicants' have allegedly resolved.

The Examiner respectfully finds Applicant's arguments unpersuasive. Regarding (1), the teaching of Keller that the ingredients may be mixed in any order would lead the ordinary skilled artisan to modify the order and thus obtain the order of the steps recited in the claimed method through optimization. Applicants' data contains no comparison with any prior art composition made using the recited steps in a different order than presented in Applicants' claims. Thus, Applicants' data and the lack of comparative data do not establish the alleged criticality of the order of the steps of the claimed method.

Regarding (2), Applicants have provided no citations of the alleged prior art that support their assertion that the preparation of ternary dry powder formulations is difficult. Thus, this allegation is unpersuasive. The instant rejection is maintained.

Regarding (3), Ward was clearly relied upon as a secondary reference to demonstrate what was well known and conventional in the art, namely that it was common to use inert carriers having a VMD of about 50 to about 250 microns. Ward clearly establishes that a VMD of about 50-250 microns is conventional for carriers in dry powder formulations.

Regarding (4), Applicants have failed to indicate when the allegedly "long felt need" was first identified. Applicants provide no data or evidence that others attempted to solve the alleged long-felt need and were unsuccessful, and that attempts to solve the "long-felt need" did not occur because of technical reasons as opposed to other factors (e.g. lack of interest in solving the problem, such as for financial reasons). Thus, Applicants have failed to establish the existence of an alleged "long-felt need." The instant rejection remains proper and is maintained.

Conclusion

Claims 1-3 and 5-32 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Supervisory Patent Examiner, Art Unit 1616